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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,375	11/14/2001	Mark M. Wang	265/084	1408
34263	7590	07/13/2004	EXAMINER	
O'MELVENY & MEYERS 114 PACIFICA, SUITE 100 IRVINE, CA 92618			KOSSON, ROSANNE	
			ART UNIT	PAPER NUMBER
			1651	

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/993,375

Applicant(s)

WANG ET AL.

Examiner

Rosanne Kosson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 November 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on _____ is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Information Disclosure Statement

The information disclosure statement (IDS) filed on March 5, 2002 lists document IY (Yuqiu) which is not present in the application file to which Applicants refer. Applicants may wish to provide a copy of this reference in order to have it considered.

Similarly, the IDS filed on May 17, 2004 lists a published PCT application and 11 non-patent literature references. These references are not present in the application file to which Applicants refer. Applicants may wish to provide a copy of these references in order to have them considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 1 recites a method for separating particles by the steps of separating particles in a medium having a dielectric constant chosen for the property of enhancing the sensitivity of the discrimination between the particles and then changing the medium to

one having a dielectric constant chosen for the property of separating the particles faster. Firstly, the claim circularly recites a method of separating particles by separating particles and does not recite a means for separating particles. Applying a focused beam of light, such as a laser beam, to a particle mixture to separate the particles by type, is critical or essential to the practice of the invention, as disclosed in the specification, but not included in the claim(s). See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

Secondly, the claim recites "a dielectric constant chosen to enhance the sensitivity of the discrimination between the particles." This phrase is not defined in the specification. Claim 1 also recites "a dielectric constant which causes faster separation between the particles," which also is not defined in the specification. A mixture of particles may be placed in a medium that has a dielectric constant selected for optimal separation of the mixture into its particle types. This medium would have chemical and physical characteristics such that optimal separation, relative to other media, is achieved when a force (or gradient of a force) is applied to the particle mixture. Using this medium, compared to using non-optimized media, it may be said that faster separation of the particles may be achieved, or that the medium is more sensitive to the applied force, allowing for greater separation of the mixture, or that the medium has a greater discriminating effect on the particle mixture, allowing for greater separation of the mixture. The specification does not teach how to make a medium that has "a dielectric constant chosen to enhance the sensitivity of the discrimination between the particles" or a medium that has "a dielectric constant which causes faster separation

between the particles,” nor does it teach what the difference is between these two types of media. The specification merely teaches that the dielectric constant of the medium may be the same as or different from the dielectric constant of one of the particle types and that, if the dielectric constants are different, they may be different by certain amounts. Additionally, the specification does not teach that, once a medium of the desired dielectric constant is chosen and used, the medium may be changed to a medium with a different dielectric constant. In the separations described in the specification (see pp. 46-51), only one medium is used for each. Consequently, the specification provides no guidance for making the claimed the claimed media, nor does it provide an indication as to when the first medium is to be changed to the second medium. For one of skill in the art to practice the claimed invention, an undue amount of experimentation would be required. Thus, a holding of non-enablement is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites “a dielectric constant chosen to enhance the sensitivity of the discrimination between the particles.” This phrase is not defined in the specification. Claim 1 also recites “a dielectric constant which causes faster separation between the particles,” which also is not defined in the specification.

Because these phrases are vague and indefinite, the meaning of claim 1 is not clear. It cannot be determined what Applicants intend to include or exclude from all the claims.

Claim 3 recites the limitation "the first particle" in the third line. There is insufficient antecedent basis for this limitation in the claim.

Claim 3 is also rejected under 35 U.S.C. 112, second paragraph, for reciting the limitation that the difference in dielectric constants between the medium and the first particle and between the particles is "substantially the same." "Substantially the same" is not defined in the specification. The difference between "substantially the same" and "the same" cannot be determined. Thus, the metes and bounds of the claim are unclear, and it cannot be determined what Applicants intend to include or exclude from the claim.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, for reciting the limitation that the dielectric constant of the medium used is "substantially equal" to the dielectric constant of one of the particles. "Substantially equal" is not defined in the specification. The difference between "substantially equal" and "equal" cannot be determined. Thus, the metes and bounds of the claim are unclear, and it cannot be determined what Applicants intend to include or exclude from the claim.

Thus, a holding of indefiniteness of claims 1-7 is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Experimental Biochemistry 2d Ed., J.M. Clark and R.L. Switzer, eds, Section II, pp. 73-74, W.H. Freeman and Co., New York, 1977. Clark and Switzer disclose that, in a mixture of protein particles, different protein particles have different dielectric constants in aqueous solutions and that these differing dielectric constants are a feature that may be used to separate the proteins in a mixture. In a given dielectric medium, some proteins will precipitate while other proteins remain in solution. The insoluble proteins may be removed and the medium changed by adding a reagent, such as a salt or water-miscible solvent. In this second medium, a second group of proteins will precipitate while others remain in solution, thereby achieving separation of protein particles. A mixture of protein particles may also be separated by ion exchange chromatography, in which the proteins in a dielectric medium are bound to a polymeric chromatographic material. The medium is changed by adding a salt to increase the dielectric constant of the medium, either step-wise or continuously. As the dielectric properties of the medium change, some proteins are eluted while others remain bound, thereby effecting separation of the protein particle mixture, either step-wise or in a continuum (see Solubility Properties and Chromatographic Separation). For a mixture of protein particles, the dielectric constant of the medium is necessarily closer to the dielectric constant of one type of particle than it is to the dielectric constant of another

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type of particle. Thus, the teachings of Clark and Switzer read on the invention as claimed in claims 1 and 2. A holding of anticipation is, therefore, required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Quake et al. (WO 99/61888) in view of Yang et al. (Biophysical J 76:3307-3314, 1999), Landa (U.S. 4,460,667), Pethig et al. (Trends Biotechnol 15(10):426-432, 1997) and Markx et al. (J Biotechnol 51:175-180, 1996). Quake discloses a method of separating a mixture of cells in which the cells are placed in a dielectric medium and there exhibit different dielectric properties according to cell type. Manipulation of cells can be

performed in a streaming fluid of the dielectric medium. Optical tweezers can be used to trap and move objects, e.g., cells, with focused beams of light such as lasers (see p. 24, line 4, to p. 25, line 13). Quake does not disclose using media that have a certain dielectric constant relative to the dielectric constant of one particle type, or relative to the difference in dielectric constants between two particle types. Yang, however, discloses separating mixtures of various types of blood cells based on their dielectric properties. The dielectric properties (membrane capacitance, internal conductivity and internal permittivity) of several types of white blood cells are determined relative to the medium in which they are contained (PBS with sucrose and dextrose). The different cell types are then separated by dielectrophoretic fractionation (see pp. 3309-3310). Landa discloses that to separate particles by differences in dielectric constants, the desired particle should have a dielectric constant higher than that of the surrounding medium. In dielectrophoresis, a particle with a dielectric constant higher than that of the surrounding medium will move in the direction of the higher field intensity (see column 8, lines 55-61). One of ordinary skill in the art would have been motivated to modify the separation method of Quake by using dielectric media in which the different cell types to be separated would have demonstrated different dielectric properties, as disclosed by Yang, because Yang discloses the desirability of using dielectric media in which the cell types may be separated. Landa provides further guidelines for selecting a dielectric medium- that the dielectric constant should be lower than that of the desired particle type and that that particle type will move a particular direction relative to the applied field- thereby emphasizing the importance of dielectric medium selection. Thus, the

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artisan of ordinary skill would have been motivated to have combined the separation method of Quake with principles of dielectric medium selection as disclosed in Yang and Landa for the advantages disclosed in Yang and Landa.

As discussed above, Quake discloses a method of separating a mixture of cells in which the cells are placed in a dielectric medium where they exhibit different dielectric properties according to cell type. Manipulation of cells can be performed in a streaming fluid of the dielectric medium, and optical tweezers can be used to trap and move objects such as cells (see p. 24, line 4, to p. 25, line 13). Quake does not disclose using media that have a certain dielectric constant relative to the dielectric constant of one particle type, or relative to the difference in dielectric constants between two particle types. Pethig, however, discloses separating mixtures of various types of cells (white blood cells, bacteria, cancerous cells vs. normal blood cells, live yeast cells vs. dead yeast cells) or macromolecules (DNA and proteins) based on their dielectric properties. The particle conductivities for a number of types of bacteria were determined relative to the medium in which they were suspended (a NaCl gradient solution, see pp. 430-431 and listed reference no. 18, Markx et al., J Biotechnol 51:175-180, 1996, enclosed). One of ordinary skill in the art would have been motivated to modify the separation method of Quake by using dielectric media in which the different cell types to be separated would have demonstrated different dielectric properties, as disclosed by Pethig, because Pethig discloses the desirability of using dielectric media in which the cell types may be separated. As discussed above, Landa provides further guidelines for selecting a dielectric medium- that the dielectric constant should be lower than that of

the desired particle type and that that particle type will move a particular direction relative to the applied field- thereby emphasizing the importance of dielectric medium selection. Thus, the artisan of ordinary skill would have been motivated to have combined the separation method of Quake with principles of dielectric medium selection as disclosed in Pethig and Landa for the advantages disclosed in Pethig and Landa. Thus, a holding of obviousness is required.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosanne Kosson whose telephone number is 571-272-2923. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


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Rosanne Kosson
Examiner
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2004-07-08



FRANCISCO PRATS
PRIMARY EXAMINER